Claims

1. A method to selectively incorporate or encapsulate proteinaceous target molecules into virus like particles (VLPs) by:
co-expressing in cells

(i) said target molecules comprising a first amino acid sequence and a second amino acid sequence and

(ii) signal molecules comprising a first amino acid sequence and a second amino acid sequence, the latter of which confers on the signal molecules the ability to assemble into virus like particles and preferably to be released into an extracellular environment,

wherein said first amino acid sequences of said signal molecules functionally operate in a non-covalent manner with said first amino acid sequences of said target molecules so as to incorporate or encapsulate said target molecules into said virus like particles.

2. The method according to claim 1 wherein said first amino acid sequences of said signal molecules functionally operate with said first amino acid sequences of said target molecules by non-covalent physical forces selected from the group consisting of van der Waals forces, electrostatic forces, stacking interactions, hydrogen bonding and steric fit.

3. The method according to claim 1 or 2 wherein said signal molecules interact with said target molecules by non-covalent physical forces having a binding constant of $K_{ass} \geq 10^{-6}$ M.

4. The method according to any of claims 1 to 3 wherein said virus like particles are released from said cell by exocytosis, lysis or budding through an appropriate cellular membrane.

5. The method according to claim 4 wherein budding is through the plasma membrane, the endoplasmatic reticulum, Golgi or nuclear membranes.

6. The method according to any of claims 1 to 5 wherein said second amino acid sequence of said target molecules is heterologous to the virus like particle.

7. The method according to claim 6 wherein said second amino acid sequence of said target molecule is chosen from the group consisting of receptors, ion channels, enzymes, adhesion molecules, components of membrane pores, and fragments or derivatives thereof.

8. The method according to claim 7 wherein said receptor is a transmembrane receptor, in particular a G-protein coupled receptor, which is incorporated into an envelope of virus like particles by a budding process.

9. The method according to claim 7 wherein said receptor is a cytosolic or nuclear receptor which is incorporated into or encapsulated by a protein capsid of a naked or enveloped virus like particle.

10. The method according to claim 6 wherein said second amino acid sequence of said target molecule is a luminescent peptide or protein.

11. The method according to any of claims 1 to 10 wherein said second amino acid sequence of said signal molecule comprises at least a fragment of a virus capsid protein, or a precursor of a virus capsid protein, or a fragment of a virus envelope protein, or a precursor of a virus envelope protein.

12. The method according to any of claims 1 to 10 wherein said second amino acid of said signal molecule comprises at least a fragment of a capsid protein of a virus like particle, or a precursor of said capsid protein, or a fragment of an envelope protein of a virus like particle, or a precursor of said envelope protein.

13. The method according to claim 11 or 12 wherein said capsid or envelope protein is derived from capsids or envelopes of virus families selected from the group consisting of retroviruses, picornaviruses, reoviruses, polyomaviruses, papillomaviruses, parvoviruses, nodaviruses, coronaviruses, herpesviruses, hepadnaviruses, baculoviruses and bacteriophages.

14. The method according to claim 13 wherein said second amino acid sequence of said signal molecule is a structural protein encoded by the *gag*-gene of retroviruses.

15. The method according to any of claims 6 to 10 wherein said second amino acid sequence of said signal molecule is encoded by at least a fragment of a retrotransposon, in particular a Ty element in yeast, a copia element in insects, a copia-like element in insects, VL 30 in mice, or an IAP gene in mice.

16. A virus like particle obtainable by the method according to any of claims 1 to 15.

17. A reagent kit comprising a virus like particle with incorporated or encapsulated target molecules according to any of claims 1 to 15.

18. A medicament or a precursor thereof comprising a virus like particle with incorporated or encapsulated target molecules according to any of claims 1 to 15.

19. The medicament or a precursor thereof according to claim 18 further comprising molecules integrated into or attached to the capsid of a naked virus like particle or the membrane of an enveloped virus like particle, said molecules having the function to direct said medicament or said precursor thereof to its area of influence.

20. Use of a virus like particle obtainable by the method according to any of

claims 1 to 15 for preparation of a medicament or a precursor thereof for treating or preventing genetic diseases, tumour diseases, autoimmune or infectious diseases.

21. Use of virus like particles obtainable by the method according to any of claims 1 to 15 in identification and characterisation of interactions between target molecules incorporated into distinct populations of virus like particles.

22. Use of virus like particles obtainable by the method according to any of claims 1 to 15 in identification and characterisation of interactions between target molecules and further molecules of interest, in particular molecules bound to the surface of cells or beads, or molecules soluble in aqueous medium, in particular molecules of intracellular functional location.

23. Use of virus like particles obtainable by the method according to any of claims 1 to 15 in identification of potentially pharmaceutically active substances.

24. Use of virus like particles obtainable by the method according to any of claims 1 to 15 in identification of analytes in diagnostic applications.

25. A method for identifying compounds that modulate cell surface protein-mediated activity by detecting intracellular transduction of a signal generated upon interaction of the compound with the cell surface protein, comprising:

- comparing the amount of reporter gene product expressed in a first recombinant cell in the presence of the compound with the amount of product in the absence of the compound, or with the amount of product in a second recombinant cell; wherein
- the first recombinant cell contains a reporter gene construct and expresses the cell surface protein;
- the second recombinant cell is identical to the first recombinant cell, except that it does not express the cell surface protein or expresses the cell sur-

face protein at a predefined level; and

- the reporter gene construct contains:
  (a) a transcriptional control element that is responsive to the intracellular signal generated by the interaction of an agonist with the cell surface protein;
  (b) a reporter gene that encodes a translational signal molecule and is in operative association with the transcriptional control element; wherein
- the translational signal molecules are able to assemble into virus like particles which are preferably released into an extracellular environment.

26. The method according to claim 25, further comprising, selecting compounds that change the amount of reporter gene product expressed in the first recombinant cell in the presence of the compound compared to the amount of product in the absence of the compound, or compared to the amount of product in the second recombinant cell.

27. The method according to claims 25 or 26 wherein the cell surface protein is a cell surface receptor, an adhesion molecule, a membrane pore, or an ion channel.

28. The method according to any of claims 25 to 27 wherein said detectable translational signal molecule further comprises a luminescent polypeptide, in particular green fluorescent protein or mutants thereof, or further comprises an entity which acts as a tag for subsequent labelling with a detectable reagent, or further comprises an enzyme.

29. The method according to any of claims 25 to 28 wherein said compound is an agonist of said cell surface protein.

30. The method according to any of claims 25 to 28 wherein said compound is an antagonist of said cell surface protein.

31. The method according to claim 30 further comprising prior to or simultaneously with comparing the difference in the amount of a reporter gene product, contacting the recombinant cell with an agonist that activates said cell surface protein, whereby said translational signal molecule is expressed.

32. The method according to any of claims 25 to 31 wherein the transcriptional control region includes at least one regulatory element selected from the group consisting of serum responsive elements, cyclic adenosine monophosphate responsive elements, and elements responsive to intracellular calcium ion levels.

33. The method according to any of claims 25 to 32 wherein said method is a homogeneous assay, in particular a homogeneous high throughput assay for screening a plurality of compounds.

34. The method according to any of claims 25 to 33 wherein said virus like particles are detected through use of microscopy or spectroscopy, in particular confocal microscopy or spectroscopy.

35. The method according to any of claims 25 to 34 wherein said virus like particles are released from said cell by exocytosis, lysis or budding through an appropriate cell membrane.

36. The method according to any of claims 25 to 35 wherein said translational signal molecule comprises at least a fragment of a virus capsid or envelope protein, or a precursor of a virus capsid or envelope protein.

37. The method according to any of claims 25 to 35 wherein said translational signal molecule comprises at least a fragment of a capsid or envelope protein of a virus like particle, or a precursor of said capsid or envelope protein.

38. The method according to claims 36 or 37 wherein said capsid or envelope

protein is derived from capsids or envelopes of virus families selected from the group consisting of retroviruses, picornaviruses, reoviruses, polyomaviruses, papillomaviruses, parvoviruses, nodaviruses, coronaviruses, herpesviruses, hepadnaviruses, baculoviruses and bacteriophages.

39. The method according to any of claims 25 to 35 wherein said translational signal molecule is encoded by at least a fragment of a retrotransposon, in particular a Ty element in yeast, a copia element in insects, a copia-like element in insects, VL30 in mice, or an IAP gene in mice.

40. A recombinant cell comprising:

- D N A that encodes a cell surface protein whose activity is modulatable by extracellular signals; and
- a reporter gene construct containing a reporter gene in operative linkage with one or more transcriptional control element that is regulated by said cell surface protein, wherein:
- said reporter gene encodes a translational signal molecule, and
- said translational signal molecules are able of assembling into virus like particles which are preferably released into an extracellular environment.

41. The cell according to claim 40 wherein the transcriptional control element includes at least one regulatory element selected from the group consisting of serum responsive elements, cyclic adenosine monophosphate responsive elements, and elements responsive to intracellular calcium ion levels.

42. The cell according to claim 40 or 41 wherein said translational signal molecule further comprises a luminescent polypeptide, in particular green fluorescent protein or mutants thereof, or further comprises an entity which acts as a tag for subsequent labelling with a detectable reagent, or further comprises an enzyme.

43. The cell according to any of claims 40 to 42 wherein said cell surface pro-

tein is a cell surface receptor, an adhesion molecule, a membrane pore, or an ion channel.

44. An assay for screening a plurality of compounds to determine the degree of inhibition or stimulation of a ligand/binding domain interaction or of an enzyme catalysed reaction by said compounds, or to determine the degree of binding of said compounds to a target molecule, or to determine the capability of said compounds to enter into a virus like particle, said assay comprising:

(a) a step selected from the group consisting of

(1) contacting said compounds to be tested with said ligand and said binding domain;

(2) contacting said compounds to be tested with said enzyme and substrate for said enzyme;

(3) contacting said compounds to be tested with said target molecule; and

(4) contacting said compounds with a virus like particle;

wherein said binding domain, or enzyme, or target molecule is incorporated into or encapsulated by virus like particles, and

wherein inhibition, stimulation or binding by or entrance of one or more of said compounds causes a change in the amount of an optically detectable label bound to or encapsulated by said virus like particles present in said assay and/or causes a change in a further property of said virus like particles;

(a) determining said degree of inhibition, stimulation, binding or entrance by:

measuring through use of optical methodologies amounts of said optically detectable label bound to or encapsulated by individual virus like particles and/or measuring the further property of said virus like particles;

comparing said amounts of said optically detectable label bound to or encapsulated by individual virus like particles with an amount of back-ground signal in said assay caused by label that is not bound to or encapsulated by said virus like particles and/or comparing said property of said virus like particle under study with the property of a reference virus like particle;

and determining said degree of inhibition, stimulation, binding or entrance from the difference between said bound/encapsulated and background signal

and/or from the difference between said property of the virus like particle under study and the property of a reference virus like particle.

45. The assay according to claim 44 wherein said optical methodology comprises methods of confocal microscopy or spectroscopy.

46. The assay according to claim 44 or 45 wherein said optically detectable label is a fluorescent ligand, or fluorescent substrate, or fluorescent product of an enzymatic reaction and said optical methodology comprises fluorescent techniques, in particular fluorescence correlation spectroscopy, fluorescence cross-correlation spectroscopy, fluorescence intensity distribution analysis, fluorescence lifetime measurements, fluorescence anisotropy measurements, fluorescence resonance energy transfer, or combinations thereof.

47. The assay according to any of claims 44 to 46 wherein a further property of said virus like particles is determined by electrical methodologies.

48. The assay according to claim 47 wherein said electrical methodology comprises impedance or dielectrophoresis measurements.

49. The assay according to any of claims 44 to 48 wherein said binding domain, or enzyme, or target molecule is incorporated into or encapsulated by said virus like particles through fusion to constituents of said virus like particle, in particular through fusion to capsid or envelope constituents.

50. The assay according to any of claims 44 to 48 wherein said binding domain, or enzyme, or target molecule is incorporated into or encapsulated by said virus like particles through non-covalent physical forces between constituents of said virus like particles and said binding domain, enzyme or target molecule.

51. The assay according to any of claims 44 to 50 wherein said assay is a

homogeneous high throughput assay.

52. An assay for screening a plurality of compounds to determine the degree of inhibition or stimulation of an interaction between at least two target molecules, said assay comprising:

(a) adding a liquid suspension of first target molecules incorporated into first virus like particles and a liquid suspension of second target molecules incorporated into second virus like particles to a plurality of containers;

(b) adding a plurality of compounds to be screened for said inhibition or stimulation individually or in combination to said plurality of containers;

(c) incubating said target molecules incorporated into said virus like particles and said compounds;

(d) measuring at least one property of said virus like particles; and

(e) determining the degree of inhibition or stimulation of said interaction between said target molecules by one or more of said compounds.

53. The assay according to claim 52 wherein said target molecules are incorporated into said virus like particles through fusion to capsid or envelope constituents of said virus like particles or through non-covalent physical forces between said constituents and said target molecules.

54. The assay according to claim 52 or 53 wherein an optically determinable property of said virus like particles is measured, preferably by methods of confocal microscopy or spectroscopy.

55. The assay according to claim 54 wherein said optically determinable property is measured by use of fluorescent techniques, in particular fluorescence correlation spectroscopy, fluorescence cross-correlation spectroscopy, fluorescence intensity distribution analysis, fluorescence lifetime measurements, fluorescence anisotropy measurements, fluorescence resonance energy transfer, or combinations thereof.

56. The assay according to any of claims 52 to 55 wherein said optically determinable property is measured by light scattering techniques.

57. The assay according to any of claims 52 to 56 wherein at least one further property of said virus like particles is determined, preferably by impedance or dielectrophoresis measurements.

58. The assay according to any of claims 52 to 57 wherein said assay is a homogeneous high throughput assay.

59. An assay for determining intracellular protein-protein interactions, said assay comprising:

(a) co-expressing in recombinant cells

(i) target molecules comprising a first amino acid sequence and a second amino acid sequence, the latter of which is a preferably luminescent reporter, and

(ii) signal molecules comprising a first amino acid sequence and a second amino acid sequence, the latter of which confers on the signal molecules the ability to assemble into virus like particles and preferably to be released into an extracellular environment,

(a) measuring the presence or absence of said preferably luminescent reporter within said virus like particles; and thereby

(b) determining the degree of protein-protein interaction between the first amino acid sequence of a target molecule and the first amino acid sequence of a signal molecule.

60. The assay according to claim 59 further comprising contacting said recombinant cells with compounds to be screened for their capability to interfere with said protein-protein interaction.

61. The assay according to claim 60 wherein the compounds to be screened are selected from the group consisting of cDNA expression libraries, genomic D

N A fragments, mRNAs, peptides, proteins and low molecular weight substances.

62. The assay according to any of claims 59 or 61 wherein said assay is homogeneous, preferably a homogeneous high throughput assay.

63. The assay according to any of claims 59 to 62 wherein the presence or absence of said preferably luminescent reporter within said virus like particles is measured by microscopy or spectroscopy, in particular confocal microscopy or spectroscopy.

64. The assay according to any of claims 59 to 63 wherein the presence or absence of said luminescent reporter within said virus like particles is measured by use of fluorescent techniques, in particular fluorescence correlation spectroscopy, fluorescence cross correlation spectroscopy, fluorescence intensity distribution analysis, fluorescence lifetime measurements, fluorescence anisotropy measurements, fluorescence resonance energy transfer, or combinations thereof.

65. An assay for identifying nucleic acid sequences which encode intracellular transport polypeptides or membrane associated translocation polypeptides, said assay comprising:

(a) providing a recombinant cell which comprises a nucleic acid that encodes a fusion protein comprising a first amino acid sequence and a second amino acid sequence, wherein said first amino acid sequence confers on the fusion proteins the ability to assemble into virus like particle and wherein said first amino acid sequence does not confer on the fusion protein to be transported to a cellular membrane and/or wherein said first amino acid sequence does not confer on said virus like particles the ability to be released into an extracellular environment by a budding process through said cellular membrane, and said second amino acid sequence is a polypeptide under study;

(b) expressing said fusion proteins;

(c) measuring the presence or absence of virus like particles in said extracellular environment; and thereby

(d) identifying nucleic acid sequences which encode intracellular transport polypeptides or membrane associated translocation polypeptides.

66. The assay according to claim 65 wherein a library of D N A molecules is screened in a plurality of recombinant cells.

67. The assay according to claim 65 or 66 wherein said first amino acid sequence is covalently linked to the C-terminus of said second amino acid sequence.

68. The assay according to any of claims 65 to 67 wherein said fusion protein comprises a luminescent reporter molecule covalently linked preferably to the C-terminus of said first amino acid sequence, in particular green fluorescent protein or mutants thereof.

69. The assay according to any of claims 65 to 68 wherein said first amino acid sequence is encoded by a mutant gene coding for a virus capsid or envelope protein, or by a mutant gene coding for a precursor of a virus capsid or envelope protein.

70. The assay according to any of claims 65 to 68 wherein said first amino acid sequence is encoded by a mutant gene coding for a capsid or envelope protein of a virus like particle, or by a mutant gene coding for a precursor of said capsid or envelope protein.

71. The assay according to any of claims 65 to 70 wherein said first amino acid sequence is a structural protein encoded by a mutant of the *gag*-gene of retroviruses.

72. The assay according to claim 71 wherein the position two after the initiation codon methionine is changed to any residue which codes for an amino acid that cannot be modified by myristoylation .

73. The assay according to any of claims 65 to 72 wherein said assay is a homogeneous assay, preferably a homogeneous high throughput assay.

74. The assay according to any of claims 65 to 73 wherein the presence or absence of virus like particles in said extracellular environment is measured by optical methods, preferably by confocal microscopy or spectroscopy.

75. The method according to any of claims 65 to 74 wherein the presence or absence of virus like particles in said extracellular environment is measured by use of fluorescent techniques, in particular fluorescence correlation spectroscopy, fluorescence cross-correlation spectroscopy, fluorescence intensity distribution analysis, fluorescence lifetime measurements, fluorescence anisotropy measurements, fluorescence resonance energy transfer, or combinations thereof.

76. A method for identifying substances that modulate receptor-, or membrane pore-, or ion channel-mediated activity by preferably detecting intracellular transduction of a signal generated upon interaction of an agonist with said receptor or ion channel, comprising:

- comparing the amount of reporter gene product expressed in a recombinant cell in the presence of the substance with the amount of product in the absence of the substance; wherein
- the first recombinant cell contains a reporter gene construct and expresses the receptor or ion channel; and
- the reporter gene construct contains:

  (a) a transcriptional control element that is responsive to the intracellular signal generated by the interaction of an agonist with the receptor, or membrane pore, or ion channel;

(b) a reporter gene that encodes a translational signal molecule and is in operative association with the transcriptional control element;

wherein the translational signal molecules are able to assemble into virus like particles which are preferably released into an extracellular environment.

77. The method according to claim 76, further comprising, comparing the amount of reporter gene product expressed in the recombinant cell in the presence of the agonist with the amount of product in the absence of the agonist.

78. The method according to claim 76 or 77, further comprising, comparing the amount of reporter gene product expressed in the recombinant cell in the presence of a first substance with the amount of reporter gene product in the presence of a second substance.

79. The method according to any of claims 76 to 78, wherein said substances are selected from the group consisting of cDNAs, genomic D N A fragments, mRNAs, vectors, peptides or proteins.

80. A recombinant cell comprising:

- D N A that encodes a receptor, or membrane pore, or ion channel; and
- a reporter gene construct containing a reporter gene in operative linkage with one or more transcriptional control element that is responsive to an intracellular signal generated by an interaction of an agonist with said receptor, or membrane pore, or ion channel, wherein:
- said reporter gene encodes a translational signal molecule, and
- said translational signal molecules are able of assembling into virus like particles which are preferably released into an extracellular environment.

81. The cell according to claim 80 wherein the transcriptional control region includes at least one regulatory element selected from the group consisting of

serum responsive elements, cyclic adenosine monophosphate responsive elements, and elements responsive to intracellular calcium ion levels.

82. The cell according to claim 80 or 81 wherein said translational signal molecule further comprises a luminescent polypeptide, in particular green fluorescent protein or mutants thereof, or further comprises an entity which acts as a tag for subsequent labelling with a detectable reagent.

83. A method for identifying substances which specifically modulate signaling pathways and/or a physiological status of a cell by influencing members of such signaling pathways, said method comprising:

- comparing the amount and/or properties of a reporter gene product expressed in a recombinant cell in the presence of the substance with the amount and/or properties of product in the absence of the substance; wherein
- said cell contains a marker or surrogate marker of said signaling pathway, and
- the production and/or properties of said reporter gene product or its release from the cell is responsive to the properties and/or amount of said marker or surrogate marker or to an intracellular signal generated by said marker or surrogate marker, and
- said reporter gene product comprises (i) a signal molecule and optionally (ii) a detectable moiety, wherein said signal molecules are able to assemble into virus like particle which are preferably released into an extracellular environment.

84. The method according to claim 83, wherein the reporter gene product is encoded by a reporter gene construct which contains a transcriptional control element that is responsive to the properties and/or concentration of said marker or surrogate marker or to an intracellular signal generated by said marker or surrogate marker.

85. The method according to claim 84, wherein the transcriptional control element includes at least one regulatory element selected from the group consisting of serum responsive elements, cyclic adenosine monophosphate responsive elements, and elements responsive to intracellular calcium ion levels.

86. The method according to any of claims 83 to 85, wherein said signal molecule comprises at least a fragment of a virus capsid or envelope protein, or a precursor of a virus capsid or envelope protein.

87. The method according to any of claims 83 to 85, wherein said signal molecule comprises at least a fragment of a capsid or envelope protein of a virus like particle, or a precursor of said capsid or envelope protein.

88. The method according to any of claims 83 to 87, wherein said capsid or envelope protein is derived from capsids or envelopes of virus families selected from the group consisting of retroviruses, picornaviruses, reoviruses, polyomaviruses, papillomaviruses, parvoviruses, nodaviruses, coronaviruses, herpesviruses, hepadnaviruses, baculoviruses and bacteriophages.

89. The method according to claim 88, wherein said signal molecule comprises a structural protein encoded by the *gag*-gene of retroviruses.

90. The method according to any of claims 83 to 89, wherein said detectable moiety comprises a luminescent polypeptide, in particular green fluorescent protein or a mutant thereof, or an entity which acts as a tag for subsequent labelling with a luminescent reagent.

91. The method according to any of claims 83 to 90, wherein said detectable moiety comprises a specific protein, in particular an enzyme.

92. The method according to any of claims 83 to 91, wherein said substance is

selected from the group consisting of low molecular weight compounds, nucleic acids, peptides/proteins, or PNAs.

93. The method according to claim 92, wherein a nucleic acid chosen from the group consisting of genomic D N A, cDNA, mRNA, antisense sequences, or a fragment or modified nucleic acid of the foregoing, or a vector is used as said substance.

94. The method according to claim 92 wherein said protein is an antibody.

95. A method to selectively incorporate or encapsulate a proteinaceous target molecule complex, comprising two or more components, into a virus like particle, or physically associate a proteinaceous target molecule complex with a virus like particle by co-expressing in cells

(i) a first component of the target molecule complex, said first component comprising a first amino acid sequence and a second amino acid sequence, and

(ii) a second component of the target molecule complex, and

(iii) signal molecules comprising a first amino acid sequence and a second amino acid sequence, the latter of which confers on the signal molecules the ability to assemble into a virus like particle and preferably to be released in an extracellular environment,

wherein said first amino acid sequences of said signal molecules functionally operate in a non-covalent manner with said first amino acid sequence of said first component of the target molecule complex so as to incorporate, or encapsulate said target molecule complex into, or associate said target molecule complex with said virus like particle.

96. The method according to claim 95 wherein said complexing components of said target molecule complex form homo-dimers, or hetero-dimers, or homo-oligomers, or hetero-oligomers.

97. The method according to claim 95 wherein said virus like particles are released from said cells by exocytosis, lysis or budding through an appropriate cellular membrane.

98. The method according to claim 97 wherein budding is through the plasma membrane, the endoplasmatic reticulum, Golgi or nuclear membranes.

99. The method according to any of claims 95 to 98 wherein said second amino acid sequence of said first component of the target molecule complex is heterologous to the virus like particle.

100. The method according to claims 95 to 99 wherein said target molecule complex comprises receptors, ion channels, enzymes, adhesion molecules, components of membrane pores, and fragments or derivatives, or subunits, or subtypes thereof.

101. The method according to claim 100 wherein said receptor is a cytosolic or nuclear receptor which is incorporated into, or encapsulated by, or physically associated with a protein capsid of a naked or enveloped virus like particle.

102. The method according to claim 100, wherein said receptor is a transmembrane receptor, in particular a G-protein coupled receptor, which is incorporated into an envelope of virus like particles by a budding process.

103. The method according to claims 100 to 102 wherein said target molecule complex comprises different subtypes of a given G-protein coupled receptor.

104. The method according to claims 100 to 103 wherein said target molecule complex comprises different classes of G-protein coupled receptor.

105. The method according to claims 100 to 104 wherein said target molecule complex comprises different accessory, ancillary, or other associated factors,

or effector molecules, in particular G-proteins.

106. The method according to claim 95 to 105 wherein said first amino acid sequences of said signal molecules functionally operate with said first amino acid sequences of said first component of the target molecule complex by non-covalent physical forces selected from the group consisting of van der Waals forces, electrostatic forces, stacking interactions, hydrogen bonding and steric fit.

107. The method according to any of claims 95 to 106 wherein said signal molecules interacts with said first component of the target molecule complex by non-covalent physical forces having a binding constant of $K_{ass} \geq 10^{-6}$ M.

108. The method according to any of claims 95 to 107 wherein said second amino acid sequences of said signal molecules comprise at least a fragment of a virus capsid protein, or a precursor of a virus capsid protein, or a mutant of a virus capsid protein, or a fragment of a virus envelope protein, or a precursor of a virus envelope protein, or a mutant of a virus envelope protein.

109. The method according to any of claims 95 to 108 wherein said second amino acid sequences of said signal molecules comprise at least a fragment of a capsid protein of a virus like particle, or a precursor of said capsid protein, or a mutant of said capsid protein, or a fragment of an envelope protein of a virus like particle, or a precursor of said envelope protein, or a mutant of said envelope protein.

110. The method according to claim 108 or 109 wherein said capsid or envelope protein is derived from capsids or envelopes of virus families selected from the group consisting of retroviruses, picornaviruses, reoviruses, polyomaviruses, papillomaviruses, parvoviruses, nodaviruses, coronaviruses, herpesviruses, hepadnaviruses, baculoviruses and bacteriophages.

111. The method according to claim 110 wherein said second amino acid sequence of said signal molecule is a structural protein encoded by the *gag*-gene of retroviruses.

112. The method according to any of claims 95 to 107 wherein said second amino acid sequence of said signal molecule is encoded by at least a fragment of a retrotransposon, in particular a Ty element in yeast, a copia element in insects, a copia-like element in insects, VL 30 in mice, or an IAP gene in mice.

113. A virus like particle obtainable by the method according to any of claims 95 to 112.

114. A reagent kit comprising a virus like particle with incorporated, or encapsulated, or physically associated target molecule complexes according to any of claims 95 to 112.

115. A medicament or a precursor thereof comprising a virus like particle with incorporated, or encapsulated, or physically associated target molecule complexes according to any of claims 95 to 112.

116. Use of virus like particles obtainable by the method according to any of claims 1 to 15 and claims 95 to 112 for the concentration, isolation, and/or purification of recombinant molecules.

117. A method according to any of the claims 1 to 15 and/or 95 to 112 for achieving enrichment of substances in a medium in which cells are arranged when the virus-like particles are released in the medium, which virus-like particles incorporate, encapsulate or are associated with the substances.

118. The method of claim 117 wherein the substances are proteins, poly- or oligonucleotides, organic molecules of lower molecular weight, ions or the like.